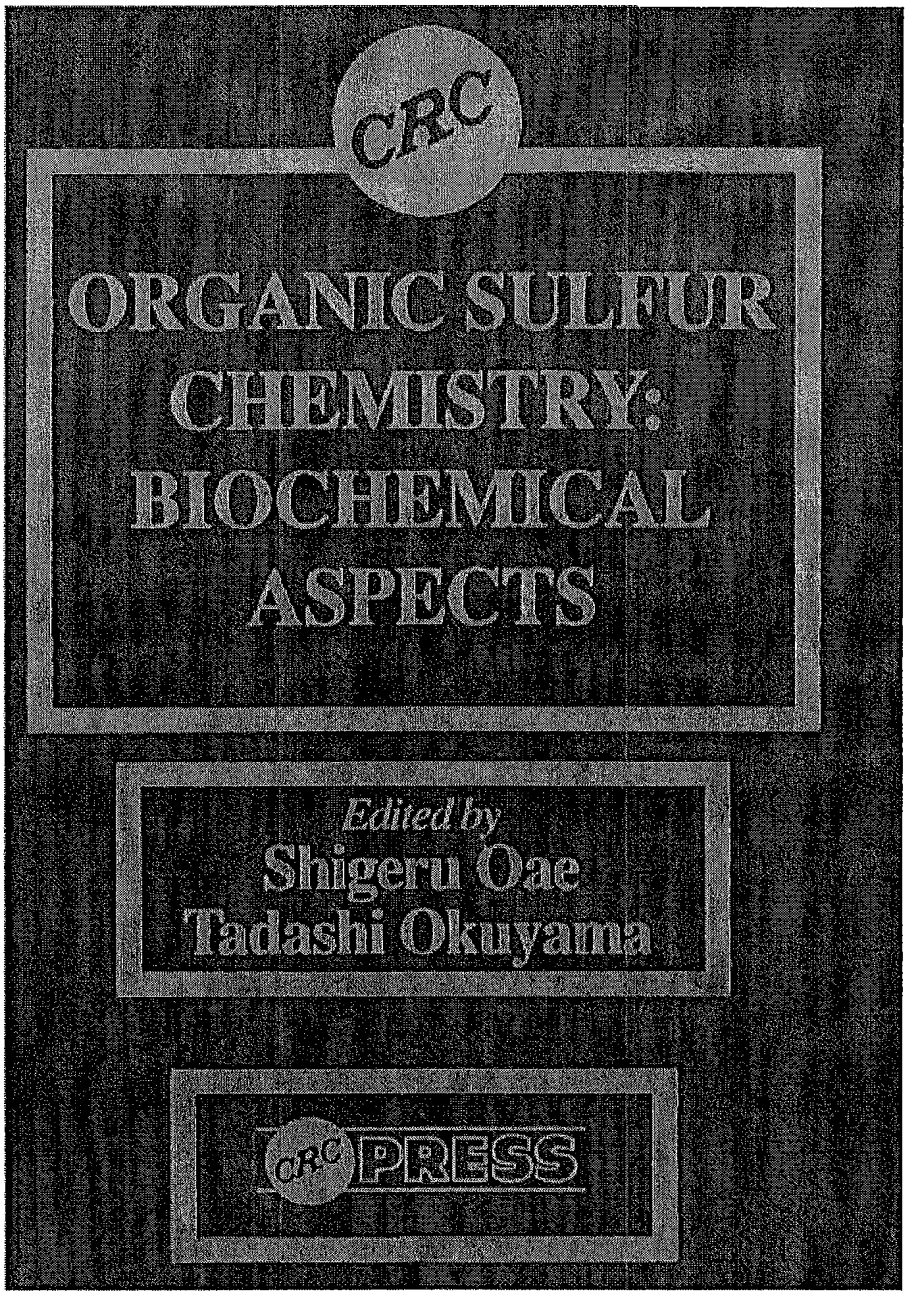
CRC
ORGANIC SULFUR CHEMISTRY: BIOCHEMICAL ASPECTS
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CRC PRESS

TABLE 1
Properties of Fully and Partially Reduced Proteins

Protein	No. of -SS-	Denaturant	No. of -SS- reduced	Conformation and Stability
Insulin (INS)	3	Yes	3	Random
		Urea	1	Native
		Analog	1	Native
Lysozyme (LNZ)	4	Yes	4	Random
		Yes	2	Slightly native
		Yes	1	Slightly native
Naerstoxin (NTX)	5	None	5	Random
		None	1	Slightly native
Papain (PAP)	3	CICT	3	Random
		Urea	1	Native
Proteinase inhibitor (potato) (PPI)	1	None	1	Native
Ribonuclease (RNS)	4	Urea	4	Slightly random
		None	2	Native
Trypsin inhibitor (pancreatic) (PTI)	3	None	3	Random
		None	1	Native
Pepsin (PEP)	3	Yes	3	Random
Trypsin inhibitor (soybean) (STI)	2	None	1	—
TRYG	6	None	1	Slightly native

157), and (128-232), where the N'- and/or C'-termini of a domain rather than the whole protein are involved. A disulfide can be classified according to the positions of its half-cystines, e.g., in lysozyme (EC 3.2.1.17) S-S, 6-127 is a 1-5 disulfide. Local disulfide connectivities with half cystines are demonstrated in detail.[11]

2. The Role of Disulfide Bridges

The role of disulfide bridges and properties of fully and partially reduced proteins collected from the literature are summarized in Table 1.[11] When all the disulfide bridges in a protein are reduced, both the structure and function are generally lost completely. For instance, fully reduced BPTI is a very disordered polymer, even in the absence of denaturants.[18] This may simply reflect the poor van der Waals contacts between the two bulky thiol groups which replace the more compact S-S bridge. These contacts could force the protein apart and cause denaturation. However, in related hemoglobins a much larger variation of side-chain volumes among buried homologous residues can be accommodated.[41]

It is likely that the increased disorder (i.e., entropy) of the reduced protein compared to the crosslinked structure will probably be a more significant contribution. Disulfide bonds reduce the conformational fluctuations in the denatured form and stabilize native proteins relative to denatured ones. It has been demonstrated[42,43] that formation of a disulfide bridge reduces the entropy of the polypeptide chain by S (Equation 3)

$$S = -R\left(\frac{3}{4}\ln n' + b\right) \qquad (3)$$

where n' = number of residues between crosslinks, b = constant (9/4 is a reasonable value), and R = gas constant, S = entropy units. As the length of the loop increases the entropy contribution to the stabilization also increases. When the disulfides form crossovers, the energy contribution becomes even larger.[43] Many proteins with disulfide are exceptionally